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Potential cost-effectiveness of a maternal Group B streptococcal vaccine in The Gambia

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Key words: *cost-effectiveness, vaccine, Group B streptococcus, Streptococcus agalactiae, neonatal infection*

Highlights

- First cost-effectiveness analysis of a potential hexavalent GBS vaccine in a low-resource setting
- A hexavalent GBS vaccine could avert 55% of Gambian cases and 768 disability adjusted life years per year

- 25 • Maximum cost-effective price per dose would be 12 US\$ (2016 US\$)
- 26 • GBS incidence was the most influential parameter on the cost effectiveness ratio.

27 **ABSTRACT**

28 **Objective:** To estimate neonatal health benefits and healthcare provider costs of a theoretical Group
29 B streptococcal (GBS) hexavalent maternal vaccination programme in The Gambia, a low-income
30 setting in West Africa.

31 **Methods:** A static decision analytic cost-effectiveness model was developed from the healthcare
32 provider perspective. Demographic data and acute care costs were available from studies in the
33 Gambia undertaken in 2012-2015. Further model parameters were taken from United Nations and
34 World Health Organisation sources, supplemented by data from a global systematic review of GBS
35 and literature searches. As vaccine efficacy is not known, we simulated vaccine efficacy estimates of
36 50-90%. Costs are reported in US dollars. Cost-effectiveness thresholds of one (US\$473, very cost
37 effective) and three (US\$1420, cost effective) times Gambian GDP were used.

38 **Results:** Vaccination with a hexavalent vaccine would avert 24 GBS disease cases (55%) and 768
39 disability adjusted life years compared to current standard of care (no interventions to prevent GBS
40 disease). At vaccine efficacy of 70%, the programme is cost-effective at a maximum vaccine price per
41 dose of 12 US\$ (2016 US\$), and very cost-effective at a maximum of \$3/dose. The total costs of
42 vaccination at \$12 is \$1,056,962 for one annual cohort of Gambian pregnant women. One-way
43 sensitivity analysis showed that GBS incidence was the most influential parameter on the cost
44 effectiveness ratio.

45 **Conclusion:** The introduction of a hexavalent vaccine would considerably reduce the current burden
46 of GBS disease in The Gambia but to be cost-effective, the vaccine price per dose would need to be
47 \$12/dose or less.

48

49

50 INTRODUCTION

51 Group B streptococcus (GBS) is a leading cause of neonatal sepsis and meningitis worldwide and can
52 lead to disabling long-term sequelae in up to 50% of meningitis survivors (1). A key focus for the 2030
53 sustainable development goals (SDGs) is to reduce the neonatal mortality rate (NMR) to 12/1000
54 livebirths in every country globally (2). The NMR in The Gambia, a low-income West-African country,
55 has remained static over the past 10 years at 28/1000 livebirths. (3) Since 44% of under-five deaths
56 occur during the neonatal period (first 28 days of life), and infection causes 51.8% of under-five
57 mortality worldwide, tackling neonatal GBS infection could significantly reduce neonatal mortality
58 (4,5).

59 Maternal vaccination against GBS is a global priority identified by the World Health
60 Organisation (WHO) (6). Several maternal multivalent GBS capsular polysaccharide (CPS) protein-
61 conjugate vaccines are currently undergoing Phase I/II randomised control trials (RCTs) in Europe,
62 the USA and South Africa (7). A multivalent protein-based vaccine is also undergoing phase I/II trials
63 in Europe. (8) Vaccines specifically for low- and middle-income countries (LMIC) are being developed
64 using tetanus toxoid (TT) conjugates which could potentially replace one of the tetanus doses given
65 in pregnancy in LMICs (7). Nevertheless, there is little information for healthcare providers about the
66 vaccine's potential cost-effectiveness in low-income countries. An important criteria for a licensed
67 GBS vaccine's adoption into Gavi, the Vaccine Alliance's portfolio, would be to demonstrate cost-
68 effectiveness in low-income countries (9).

69 Previous cost-effectiveness studies of GBS vaccines (10) in low-income African countries such
70 as Ghana exist but these models exclude countries such as the Gambia, which have far lower Gross
71 Domestic Product (GDP), health spending and access to care than Ghana (which achieved middle
72 income status in 2012) (11). The Gambia has relatively good health and cost information that allows
73 the potential impact of a GBS vaccine to be evaluated (12,13). This study aims to more accurately

74 inform policymakers on the potential economic impacts and neonatal health benefits of a maternal
75 multivalent GBS vaccination programme in the Gambia, an example of a low-income West-African
76 country.

77

78 **METHODS**

79 **Target population, subgroups, setting**

80 Demographic data from a previously conducted prospective study of 750 mother-infant pairs from
81 two government health centres in urban Western Gambia in 2014 (12,500 livebirths annually)
82 identified risk factors for GBS colonisation, transmission to neonates and GBS disease. New-borns
83 were followed until 90-days of age for disease, mortality and disability outcomes. There was one case
84 of culture-positive GBS disease, giving an incidence of 1.3/1000 livebirths (12). This data represents
85 a sample of convenience and the government hospitals selected represent the standard of care
86 available to Gambian women and is thus representative of neonatal care in the Gambia (13,14).

87

88 Where GBS data from this cohort was unavailable, the following hierarchy of data were selected:
89 local data from a neonatal infection study (13) and a cost analysis of pneumococcal disease
90 treatment (15), country-specific data from the Institute for Health Metrics Evaluation (IHME), UN
91 International Children's Emergency Fund (UNICEF) and WHO global health observatory (GHO)
92 (3,5,14) (Table 1). For the remaining parameters, a literature review on PubMed was conducted (15–
93 19). **[Appendix 1 and 2]**

94

95 **Disability adjusted life year (DALY) measures**

96 DALYs associated with each disease sequelae were calculated using disability weights from The Global
97 Burden of disease (GBD) study 2016 (20). GBS-specific weights are unavailable so non-specific proxies

98 were used for each disease presentation. (20,21) **[Table 1]**. Life expectancy for those with disability
99 was assumed to be 30 years based on neighbouring Senegal (22). The rates of GBS sequelae including
100 from meningitis were sourced from other studies as long-term sequelae were unavailable in the
101 Gambia (17,19,23).

102

103 **Costs of disease treatment**

104 Costs of treating neonatal patients were taken from a cohort study of neonatal sepsis at the Edward
105 Frances Small Teaching Hospital from 2014 (13). As no separate costs for the treatment of pneumonia
106 or meningitis or costs of sequelae of meningitis were available from this study, costs were taken from
107 cost-effectiveness analysis of treating young infant and paediatric patients aged 4-24 months with
108 pneumococcal disease in the Gambia, as the costs of treating GBS disease in neonates and young
109 infants was deemed to be similar, based on similar length of treatment and cost of sequelae other
110 than death (15). Family out-of-pocket costs for the care of GBS survivors were also sourced from this
111 study. All prices were inflated to 2016 US\$ using standard annual inflation rates (24). The length of
112 stay was adjusted for neonates using local data on neonatal stay for non-specific meningitis,
113 pneumonia and sepsis (13). **[Appendix 3]**

114

115 **Intervention** - Vaccine uptake was assumed to be 84.3%, the same as that for the tetanus toxoid (TT)
116 vaccine in the Gambian study (12), assuming single dose late-third-trimester vaccination to replace
117 one tetanus toxoid dose as per WHO recommendations (25). Vaccine wastage rate is assumed to be
118 10% (26). The vaccine efficacy is currently unknown, so the model was run at efficacies of 50%, 70%
119 and 90% (10). Multiplying the estimated 97% serotype coverage of a multivalent vaccine by these
120 efficacy rates provided a range of vaccine coverage from 48.5% - 87.3% for term infants. Vaccine

121 efficacy for pre-terms was calculated to be 83.1% of the efficacy for term babies. **[Appendix 4]** The
122 maximum cost-effective price per dose includes the cold storage for a new vaccine.

123

124 **Study perspective** – The study is written from the perspective of the healthcare provider with
125 additional out-of-pocket costs for families caring for affected neonates, explored in further analysis.

126

127 **The model**

128 A decision-analytic model was developed in *R* (fig. 1) from an existing UK model of GBS
129 vaccination introduction (27). The model estimates a maximum vaccine price per dose threshold
130 whereby a hexavalent CPS-TT third trimester GBS vaccination programme would be deemed cost-
131 effective in the Gambia using GDP per capita calculations. The programme is deemed *cost-effective*,
132 at a cost/DALY averted of less than 1420 US\$, three times the Gambian Gross Domestic Product per
133 capita (GDPpc) and *very cost-effective* if the cost/DALY averted is less than 473 US\$, one times GDPpc
134 (28,29).

135 The model assesses infant health outcomes from birth to 90 days of age of no intervention
136 compared to the proposed strategy of vaccination. Beyond one year after birth, an annual discount
137 rate of 3% (26) was applied to infant life years lost and healthcare costs for GBS disease survivors
138 (27). Key model inputs for the base-case population are in **Table 1**.

139

140 A decision tree, created on *LucidChart*, illustrates the individual state-transition model with either
141 strategy via embedded Markov nodes. The expectant mother can either be vaccinated or not. Each
142 livebirth may be preterm or term infants who are GBS disease-free or GBS disease sufferers, defined
143 as pneumonia, meningitis or sepsis (30). The infant is assumed to suffer from sepsis, meningitis or
144 pneumonia independently and may recover without sequelae, disabling sequelae or death. Both

145 early (EOD) and late-onset disease (LOD) are generalised as GBS disease, as Gambian data was
146 unavailable. We were unable to undertake situational analysis of stillbirths in the Gambia because
147 this association was not investigated during any of the cohort studies. **[Fig. 1.]** The results are
148 reported using the CHEERS checklist (31)

149

150 **Sensitivity analysis**

151 A one-way sensitivity analysis was carried out to show the uncertainty associated with each
152 key parameter and its impact on the cost-effectiveness of the programme. One parameter at a time
153 was varied to the maximum and minimum values of its range **[table 1]** whilst all other parameters
154 were held to their base-case values. Probabilistic sensitivity analysis was used to determine the level
155 of uncertainty associated with the calculated cost-effectiveness threshold by varying parameters
156 simultaneously whilst keeping vaccine price per dose fixed. Cost-effectiveness acceptability curves
157 were generated from 5000 simulated outcomes for prices \$3 and \$12.

158

159 **Ethics Approval**

160 This study was approved by the joint MRC Gambian Government research ethics committee,
161 L2018.61, SCC 1350v4.

162

163 **RESULTS**

164 **No intervention**

165 With no intervention, at a GBS disease incidence in the Gambia of 1.3/1000 livebirths (12), an
166 annual cohort of 89,000 livebirths (32) would face 116 cases: 25 babies would suffer from meningitis;
167 50 babies from sepsis; and 41 from pneumonia. 14 babies would have sequelae (meningitis=5,
168 sepsis=9). There would be 44 GBS deaths (meningitis=5, pneumonia=14, sepsis=25) and 1384 DALYs.
169 The total costs of no intervention for the healthcare provider are \$15,373, which comprises hospital
170 admission, hospital length of stay of 6, 10 and 11 days for babies with sepsis, pneumonia and
171 meningitis respectively and the costs of antibiotics and fluid support. **[Appendix 4]** Family out-of-
172 pocket costs would be \$5,270; \$376 per family caring for a child with GBS sequelae **[Table 2]**.

174 **Vaccination outcomes**

175 At a calculated base-case vaccine efficacy for term infants of 70% and when serotype coverage is
176 97%, GBS vaccination could avert 55% of all outcomes, i.e. 768 DALYs, 64 GBS disease cases, seven
177 GBS sequelae and 24 neonatal/young infant deaths. The provider treatment costs averted with
178 vaccination are \$6937, \$9738 and \$12,704 at vaccine efficacies 50%, 70% and 90% respectively. The
179 family out-of-pocket cost savings range between \$2084, \$2926 and \$3817 for vaccine efficacies 50%,
180 70% and 90% respectively. This represents twice to four times the annual minimal wage in the
181 Gambia of \$1610 (33). The total programme costs for 89,000 pregnancies in one year would be
182 \$1,056,962 per year. There are very modest GBS disease treatment cost savings for the healthcare
183 provider of \$9738 per year. Total family out of pocket costs per year (outside of the cost-effectiveness
184 calculation) are reduced by \$2926 per year.

186 **Cost-effectiveness**

187 Assuming 70% vaccine efficacy, the maximum cost-effective price per dose is \$12 per dose.
188 The cost/DALY averted would be \$1355, below the benchmark of three times the Gambian GDP per
189 capita (\$1420). [Table 3] This maximum cost-effective price per dose would range from \$8 to \$16 at
190 vaccine efficacies of 50% and 90% respectively.

191 At \$3/dose, the vaccination programme is very cost-effective at \$365/DALY averted assuming
192 70% vaccine efficacy which is below the benchmark cost of \$474 (GDPpc in the Gambia). **[Fig. 2]** The
193 incremental cost of the programme is \$264,658. The treatment cost savings (\$8534) are independent
194 of vaccine price per dose. The total programme costs are \$295,404.

195

196 **Sensitivity analysis**

197 The tornado diagram **[Fig. 3.]** shows that the most influential parameter is the vaccine price per dose.
198 At \$2 per dose, the cost effectiveness ratio (CER) is \$253/DALY averted and at \$20 per dose, the CER
199 is \$2233/DALY averted. GBS incidence is the second most influential parameter. At a low GBS
200 incidence (0.73/1000 livebirths), the CER is more than double at \$2419/DALY averted. The least
201 influential parameters are GBS disease treatment costs. For example, treating pneumonia at \$88.8-
202 \$159 leads to a CER ranging from \$1354-1352.

203 For the base case scenario, probabilistic sensitivity analysis was carried out at vaccine prices of \$3
204 and \$12 per dose. According to uncertainty guidelines, at least 90% of iterations need to be under
205 the CER of \$1419.6 (34). At \$3/dose, 99.92% of iterations are below this threshold, while at a vaccine
206 price per dose of \$12, 18.12% of iterations fall under the CER. These outcomes demonstrate the
207 influence of vaccine price on the GBS vaccine cost-effectiveness. **[Fig. 4.]**

208 Comparing the impact of disease incidence and vaccine efficacy on the results of the
209 probabilistic sensitivity analysis, **Fig. 5.** shows that vaccine efficacy is the most influential of the two.
210 Table 1 displays parameter values tested.

211 The cost-effectiveness acceptability curve in **Fig. 6.** shows how likely vaccination is to be cost-
212 effective over doing nothing as willingness and ability to pay increases from 0 to \$6000/DALY. While
213 over 80% of iterations are cost-effective for willingness to pay of at least \$1000/DALY when vaccine
214 price is at \$3/dose, a vaccine price of \$12/dose means that similar cost-effectiveness levels are
215 achieved at a willingness to pay of at least \$3000/DALY.

216

217 **DISCUSSION**

218 Over a one-year period, an affordable, effective maternal GBS vaccine could prevent 768
219 DALYs, 64 cases, 24 neonatal and infant deaths and seven severely disabled survivors (55% of disease-
220 burden) at a base-case vaccine efficacy of 70% in the Gambia. For higher vaccine efficacy of 90%, up
221 to 72% of the disease burden could be prevented. However, we found that the costs of the standard
222 of care for GBS were very modest, which reflects the limited facility to treat affected babies beyond
223 antibiotic administration.

224 In order to be cost-effective, our model suggests that such a vaccine would have to be
225 provided at a low cost of approximately \$12 per dose at 70% efficacy (\$8 and \$16 for 50% and 90%
226 efficacy respectively) and \$3 assuming a threshold of the Gambian GDP per capita. The net annual
227 cost of a GBS vaccination programme at \$12 per dose would be \$1,056,962. A three times GDP per
228 capita threshold allows comparison of our study with others but this threshold may be an
229 unrealistic option for The Gambia where budgets are especially constrained and resources may be
230 allocated to other sectors (17,35). It is clear from this and other GBS cost-effectiveness studies in
231 LMICs, that only modest vaccine prices could be supported, and affordability should be an
232 important criterium for vaccine development. Our cost-effective price of \$12 per dose and highly
233 cost-effective price of \$3 per dose is in line with other vaccinations provided to GAVI-eligible
234 countries. For example, the pneumococcal conjugate vaccine (PCV 13) provided by Pfizer, also

recommended by the WHO for pregnant women is priced at \$2.90 per dose to the 73 GAVI eligible countries (36) and the pentavalent vaccine (tetanus, haemophilus influenzae type B, diphtheria, pertussis and hepatitis B is available to GAVI-eligible countries at \$3/dose (37)

238

Published studies have estimated a higher threshold price for a GBS vaccine. In South Africa at a vaccine price per dose of \$20, the cost-effectiveness ratio at 70% vaccine efficacy is \$1533 per DALY averted (10). In the Gambia, if the same vaccine price was used the CER would be \$2231 per DALY averted. As there is a higher base-case-value of neonatal GBS disease incidence in South Africa (a middle-income country), the ability of the vaccine to prevent disease appears greater. This, combined with their higher treatment costs, leads to greater cost savings after introducing the vaccine in South Africa than in the Gambia (10).

There are several differences between our CEA and other models. Firstly, our study used the data from a neonatal and infant cohort to provide information on GBS disease. We included an estimate of GBS attributable pneumonia (10,17,38), which was not included in other cost-effectiveness analyses of GBS vaccines. As most infants with pneumonia will die without prompt recognition and treatment, the addition of pneumonia is important in reducing the burden of death in the neonatal and early infant period (39). The most influential factor in our sensitivity analysis was disease incidence, indicating that investments in surveillance are most likely to reduce uncertainty on cost-effectiveness.

The sub-Saharan Africa (SSA) study clustered countries with similar socio-economic backgrounds together making generalised assumptions about healthcare settings. (17) Using Ghana as an example of a low income country, the maximum cost-effective vaccine price per dose is \$7 at \$350/DALY averted at a vaccine efficacy of 70%. (17) When our study is adjusted to these assumptions, however, the CER is \$544/DALY which is higher than this estimate likely due to our

259 lower disease incidence. Both previous studies assumed effectiveness from a trivalent vaccine, yet
260 without serotype V, which is included in our study, such a vaccine would be less cost-effective in the
261 Gambia. Differences in income and treatment costs in both the South Africa and the SSA study make
262 comparisons between these studies and ours difficult. For example, in South Africa, the average
263 length of hospital stay for neonatal meningitis was 17 days whilst in both the SSA and our study the
264 median length of stay was 11 days. (15,40).

265 In comparison to other vaccines in the infant extended programme on immunisation in the
266 Gambia, a GBS vaccine could be more cost-effective than the 13-valent pneumococcal conjugate
267 vaccine (PCV). The PCV cost-effectiveness study measured the same disease presentations as our
268 study, but only 65% of DALYs were averted compared to 72% for the GBS vaccine at 90% vaccine
269 efficacy using similarly conservative estimates, making an effective case for the introduction of this
270 hexavalent vaccine to prevent all forms of GBS disease in the Gambia. (26)

271 There are limitations to this study. This analysis is based on a single study of 750 women
272 delivering in coastal Gambia and, although this is the largest study of GBS disease in a low income
273 setting, may not be representative of GBS incidence in the whole of the Gambia or other low
274 income countries. Nonetheless the incidence used in our model is consistent with estimates of
275 disease burden for Western Africa (41) We included only adult pregnant women and as 8.8% of
276 pregnancies in the Gambia occur in women aged between 15-19 years our study may have
277 underestimated vaccine impact in this vulnerable group as low maternal age is a risk factor for
278 neonatal GBS disease (42,43). The static model used, which has been used for other cost
279 effectiveness studies of GBS vaccine, does not enable us to assess potential changes in the
280 incidence of GBS over time, or any indirect vaccine effects. Several other factors will affect the
281 model and our results may therefore underestimate the cost-saving of a GBS vaccine. Firstly, the
282 surveillance occurred over one year, and subsequent years may have revealed an increased disease

incidence which would increase the cost-effectiveness of our model. We were unable to include indirect costs as these are not currently defined for maternal vaccination. Finally, although we added family out of pocket costs to our model, we were unable to include all societal costs. For parameters such as neurodevelopmental impairment, country-specific data was not available, thus our estimates are derived from global estimates that may not represent The Gambia (19). However, the degree of disability due to GBS meningitis is similar to that of other bacterial meningitis in similar settings and this data was available from the Gambia.(15,23) Additionally, only GBS moderate-severe sequelae were included because data on mild sequelae rates are less reliable, especially in the Gambia. (19). Consequently, the model may underestimate some cases with sequelae and their associated DALYs. While treatment costs in our model were modest, we acknowledge that the length of hospital stay may vary for different causative pathogens. Only non-pathogen specific costs were available since in most cases, blood cultures would not be taken because of constrained resources and the reliance on families to pay for these tests. We did not evaluate other options for GBS prevention and control as these were not available during the cohort study. There is limited data on the implementation of IAP in labour in the Gambia. The PregnAnZI trial (44) randomised 830 pregnant women in labour to have either a placebo or single-dose oral azithromycin in Western Gambia and found that GBS colonisation was almost eliminated in mothers after azithromycin treatment. Azithromycin is more feasible than intravenous RFB-IA intravenous as it can be effective as late as two hours before delivery. Although this strategy has the potential to address EOD, more information is needed regarding its impact on antimicrobial resistance, the infant microbiome and other health outcomes before such a strategy can be widely recommended (44). The strategy would not reduce the burden of late onset disease, which most commonly presents as meningitis, so this burden would remain. Should this IAP strategy come into practice in the Gambia, its cost effectiveness should be compared to vaccination.

307

308 **Conclusion**

309 A vaccine that is modestly priced is likely to be a cost-effective intervention in reducing GBS disease
310 in the Gambia. Uncertainty regarding cost-effectiveness can be reduced by improving estimates on
311 the burden of GBS disease, particularly disease incidence.

312

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318

319 **Author contributions**

320 KLD and CT conceived the original idea and commented on the manuscript. NA undertook the model
321 design, analysis and manuscript drafting, KG had expert input into the model and commented on the
322 manuscript, EC, BK, UE and UO had expert input into the manuscript. All authors approved the final
323 manuscript draft.

324

325 **Conflict of interests**

326 NA, KG, KLD, EU, UO, EC, and CT declare no conflict of interests. BK is an advisor for Pfizer regarding
327 GBS vaccines.

328

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336

337 **REFERENCES**

338

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340

- 341 1. Nuccitelli A, Rinaudo C, Maione D. Group B Streptococcus vaccine: state of the art.
342 *Therapeutic Advances in Vaccines*. [Online] 2015;3(3): 79–90. Available from:
343 doi:10.1177/2051013615579869 [Accessed: 8th October 2018]
- 344 2. Chou D, Daelmans B, Jolivet RR, Kinney M, Say L, Every Newborn Action Plan (ENAP) and
345 Ending Preventable Maternal Mortality (EPMM) working groups. Ending preventable
346 maternal and newborn mortality and stillbirths. *BMJ (Clinical research ed.)*. [Online] British
347 Medical Journal Publishing Group; 2015;351: h4255. Available from: doi:10.1136/BMJ.H4255
348 [Accessed: 23rd May 2018]
- 349 3. UNICEF. *Statistics / At a glance: Gambia / UNICEF*. [Online] Available from:
350 https://www.unicef.org/infobycountry/gambia_statistics.html [Accessed: 7th May 2018]
- 351 4. Tann CJ, Martinello KA, Sadoo S, Lawn JE, Seale AC, Vega-Poblete M, et al. Neonatal
352 Encephalopathy With Group B Streptococcal Disease Worldwide: Systematic Review,
353 Investigator Group Datasets, and Meta-analysis. *Clinical Infectious Diseases*. [Online] Oxford
354 University Press; 2017;65(suppl_2): S173–S189. Available from: doi:10.1093/cid/cix662
355 [Accessed: 16th March 2018]
- 356 5. Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE, et al. Global, regional, and national causes of
357 child mortality in 2000–13, with projections to inform post-2015 priorities: an updated
358 systematic analysis. *The Lancet*. [Online] Elsevier; 2015;385(9966): 430–440. Available from:
359 doi:10.1016/S0140-6736(14)61698-6 [Accessed: 7th May 2018]
- 360 6. WHO. WHO | GBS vaccine research and development technical roadmap and WHO Preferred

- Product Characteristics. *WHO*. [Online] World Health Organization; 2017; Available from: https://www.who.int/immunization/research/development/ppc_groupb_streptovaccines/en/ [Accessed: 1st February 2019]
7. Serocorrelates of protection against infant group B streptococcus disease. *The Lancet Infectious Diseases*. [Online] Elsevier; 2019;19(5): e162–e171. Available from: doi:10.1016/S1473-3099(18)30659-5 [Accessed: 9th July 2019]
 8. Minervax. *Minervax - Frontpage*. [Online] Available from: <http://minervax.com/> [Accessed: 18th August 2019]
 9. Kallenberg J. *Gavi's Vaccine Investment Strategy*. [Online] [Accessed: 13th February 2019]. Available from: www.gavi.org [Accessed: 13th February 2019]
 10. Kim S-Y, Russell LB, Park J, Verani JR, Madhi SA, Cutland CL, et al. Cost-effectiveness of a potential group B streptococcal vaccine program for pregnant women in South Africa. *Vaccine*. [Online] Elsevier; 2014;32(17): 1954–1963. Available from: doi:10.1016/J.VACCINE.2014.01.062 [Accessed: 11th April 2018]
 11. The World Bank. *Ghana Overview*. [Online] Available from: <https://www.worldbank.org/en/country/ghana/overview> [Accessed: 7th July 2019]
 12. Le Doare K, Jarju S, Darboe S, Warburton F, Gorringer A, Heath PT, et al. Risk factors for Group B Streptococcus colonisation and disease in Gambian women and their infants. *Journal of Infection*. [Online] W.B. Saunders; 2016;72(3): 283–294. Available from: doi:10.1016/J.JINF.2015.12.014 [Accessed: 9th April 2018]
 13. Okomo UA, Dibbasey T, Kassama K, Lawn JE, Zaman SMA, Kampmann B, et al. Neonatal admissions, quality of care and outcome: 4 years of inpatient audit data from The Gambia's teaching hospital. *Paediatrics and International Child Health*. [Online] Taylor & Francis; 2015;35(3): 252–264. Available from: doi:10.1179/2046905515Y.0000000036 [Accessed:

- 385 13th March 2019]
- 386 14. United Nations Population Division. *World Population Prospects - Population Division - United*
387 *Nations*. [Online] Available from:
388 <https://esa.un.org/unpd/wpp/Download/Standard/Fertility/> [Accessed: 12th April 2018]
- 389 15. Usuf E, Mackenzie G, Sambou S, Atherly D, Suraratdecha C. The economic burden of
390 childhood pneumococcal diseases in The Gambia. *Cost Effectiveness and Resource Allocation*.
391 [Online] BioMed Central; 2016;14(1): 1–10. Available from: doi:10.1186/s12962-016-0053-4
- 392 16. Ranjeva SL, Warf BC, Schiff SJ. Economic burden of neonatal sepsis in sub-Saharan Africa.
393 *BMJ Global Health*. [Online] BMJ Specialist Journals; 2018;3(1): e000347. Available from:
394 doi:10.1136/bmjgh-2017-000347 [Accessed: 1st May 2018]
- 395 17. Russell LB, Kim S-Y, Cosgriff B, Pentakota SR, Schrag SJ, Sobanjo-ter Meulen A, et al. Cost-
396 effectiveness of maternal GBS immunization in low-income sub-Saharan Africa. *Vaccine*.
397 [Online] Elsevier; 2017;35(49): 6905–6914. Available from:
398 doi:10.1016/J.VACCINE.2017.07.108 [Accessed: 8th March 2018]
- 399 18. Kuznik A, Iliyasu G, Lamorde M, Mahmud M, Musa BM, Nashabaru I, et al. Cost-effectiveness
400 of expanding childhood routine immunization against *Neisseria meningitidis* serogroups C, W
401 and Y with a quadrivalent conjugate vaccine in the African meningitis belt. *PLoS ONE*.
402 [Online] 2017;12(11). Available from: doi:10.1371/journal.pone.0188595
- 403 19. Kohli-Lynch M, Russell NJ, Seale AC, Dangor Z, Tann CJ, Baker CJ, et al. Neurodevelopmental
404 Impairment in Children After Group B Streptococcal Disease Worldwide: Systematic Review
405 and Meta-analyses. *Clinical Infectious Diseases*. [Online] Oxford University Press;
406 2017;65(suppl_2): S190–S199. Available from: doi:10.1093/cid/cix663 [Accessed: 22nd
407 March 2018]
- 408 20. Global Burden of Disease Collaborative Netowrk. *Global Burden of Disease Study 2016 (GBD*

- 409 2016) *Disability Weights / GHDx*. [Online] Seattle, United States. Available from:
 410 [http://ghdx.healthdata.org/record/global-burden-disease-study-2016-gbd-2016-disability-](http://ghdx.healthdata.org/record/global-burden-disease-study-2016-gbd-2016-disability-weights)
 411 [weights](http://ghdx.healthdata.org/record/global-burden-disease-study-2016-gbd-2016-disability-weights) [Accessed: 7th May 2018]
- 412 21. Institute for Health Metrics and Evaluation. *The Gambia / Institute for Health Metrics and*
 413 *Evaluation*. [Online] Available from: <http://www.healthdata.org/gambia> [Accessed: 12th
 414 April 2018]
- 415 22. Griffiths UK, Dieye Y, Fleming J, Hajjeh R, Edmond K. Costs of Meningitis Sequelae in Children
 416 in Dakar, Senegal. *The Pediatric Infectious Disease Journal*. [Online] 2012;31(11): e189–e195.
 417 Available from: doi:10.1097/INF.0b013e3182615297 [Accessed: 18th May 2018]
- 418 23. Christie D, Rashid H, El-Bashir H, Sweeney F, Shore T, Booy R, et al. Impact of meningitis on
 419 intelligence and development: A systematic review and meta-analysis. Lidzba K (ed.) *PLOS*
 420 *ONE*. [Online] Public Library of Science; 2017;12(8): e0175024. Available from:
 421 doi:10.1371/journal.pone.0175024 [Accessed: 1st February 2019]
- 422 24. The World Bank. *Inflation, GDP deflator (annual %) / Data*. [Online] Available from:
 423 <https://data.worldbank.org/indicator/NY.GDP.DEFL.KD.ZG?locations=GM> [Accessed: 20th
 424 December 2018]
- 425 25. Kobayashi M, Schrag SJ, Alderson MR, Madhi SA, Baker CJ, Sobanjo-ter Meulen A, et al. WHO
 426 consultation on group B Streptococcus vaccine development: Report from a meeting held on
 427 27–28 April 2016. *Vaccine*. [Online] Elsevier; 2016; Available from:
 428 doi:10.1016/J.VACCINE.2016.12.029 [Accessed: 16th March 2018]
- 429 26. Usuf E, Mackenzie G, Lowe-jallow Y, Boye B, Atherly D. Costs of vaccine delivery in the
 430 Gambia before and after , pentavalent and pneumococcal conjugate vaccine introductions.
 431 *Vaccine*. [Online] Elsevier Ltd; 2014;32(17): 1975–1981. Available from:
 432 doi:10.1016/j.vaccine.2014.01.045

27. Giorgakoudi K, O'Sullivan C, Heath PT, Ladhani S, Lamagni T, Ramsay M, et al. Cost-effectiveness analysis of maternal immunisation against group B Streptococcus (GBS) disease: A modelling study. *Vaccine*. [Online] Elsevier; 2018;36(46): 7033–7042. Available from: doi:10.1016/J.VACCINE.2018.09.058 [Accessed: 19th August 2019]
28. The World Bank. *GDP per capita (current US\$) | Data*. [Online] Available from: <https://data.worldbank.org/indicator/NY.GDP.PCAP.CD> [Accessed: 6th May 2018]
29. Edejer T, Baltussen R, Adam T, Hutusbessy R. *WHO Guide to cost-effectiveness analysis*. [Online] 2003 [Accessed: 17th May 2018]. Available from: http://www.who.int/choice/publications/p_2003_generalised_cea.pdf [Accessed: 17th May 2018]
30. Sinha A, Russell LB, Tomczyk S, Verani JR, Schrag SJ, Berkley JA, et al. Disease Burden of Group B Streptococcus Among Infants in Sub-Saharan Africa. *The Pediatric Infectious Disease Journal*. [Online] 2016;35(9): 933–942. Available from: doi:10.1097/INF.0000000000001233 [Accessed: 15th April 2018]
31. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. *BMJ*. [Online] British Medical Journal Publishing Group; 2013;346: f1049. Available from: doi:10.1136/BMJ.F1049 [Accessed: 10th April 2019]
32. Country meters. *Live Gambia population (2018). Current population of Gambia — Countrymeters*. [Online] Available from: <http://countrymeters.info/en/Gambia> [Accessed: 17th May 2018]
33. Minimum-Wage.org. *The Gambia Minimum Wage - World Minimum Wage Rates 2019*. [Online] Available from: <https://www.minimum-wage.org/international/the-gambia> [Accessed: 8th July 2019]

- 457 34. *From 12 June 2013 JOINT COMMITTEE ON VACCINATION AND IMMUNISATION Code of*
458 *Practice June 2013.* [Online] [Accessed: 22nd August 2019]. Available from:
459 [http://www.bis.gov.uk/assets/goscience/docs/c/11-1382-code-of-practice-scientific-](http://www.bis.gov.uk/assets/goscience/docs/c/11-1382-code-of-practice-scientific-advisory-committees.pdf)
460 [advisory-committees.pdf](http://www.bis.gov.uk/assets/goscience/docs/c/11-1382-code-of-practice-scientific-advisory-committees.pdf) [Accessed: 22nd August 2019]
- 461 35. Marseille E, Larson B, Kazi DS, Kahn JG, Rosen S. Thresholds for the cost–effectiveness of
462 interventions: alternative approaches. *Bulletin of the World Health Organization.* [Online]
463 2015;93(2): 118–124. Available from: doi:10.2471/BLT.14.138206 [Accessed: 24th May 2018]
- 464 36. *Pneumococcal vaccine price drops for third year running.* [Online] Available from:
465 [https://www.gavi.org/news/media-room/pneumococcal-vaccine-price-drops-third-year-](https://www.gavi.org/news/media-room/pneumococcal-vaccine-price-drops-third-year-running)
466 [running](https://www.gavi.org/news/media-room/pneumococcal-vaccine-price-drops-third-year-running) [Accessed: 16th January 2020]
- 467 37. *GAVI’s impact on vaccine market is bringing down prices.* [Online] Available from:
468 <https://www.gavi.org/news/media-room/gavis-impact-vaccine-market-bringing-down-prices>
469 [Accessed: 16th January 2020]
- 470 38. Kim S-Y, Nguyen C, Russell LB, Tomczyk S, Abdul-Hakeem F, Schrag SJ, et al. Cost-
471 effectiveness of a potential group B streptococcal vaccine for pregnant women in the United
472 States. *Vaccine.* [Online] Elsevier; 2017;35(45): 6238–6247. Available from:
473 doi:10.1016/J.VACCINE.2017.08.085 [Accessed: 7th March 2018]
- 474 39. Duke T. Neonatal pneumonia in developing countries. *Archives of disease in childhood. Fetal*
475 *and neonatal edition.* [Online] BMJ Publishing Group; 2005;90(3): F211-9. Available from:
476 doi:10.1136/adc.2003.048108 [Accessed: 9th July 2019]
- 477 40. WHO. Pocket Book of Hospital Care for Children: Guidelines for the Management of Common
478 Childhood Illnesses. *Guidelines for the management of common illnesses.* [Online] 2013;
479 125–143. Available from: doi:<http://dx.doi.org/10.1016/j.cardfail.2011.02.010>
- 480 41. Seale AC, Bianchi-Jassir F, Russell NJ, Kohli-Lynch M, Tann CJ, Hall J, et al. Estimates of the

- 481 Burden of Group B Streptococcal Disease Worldwide for Pregnant Women, Stillbirths, and
482 Children. *Clinical Infectious Diseases*. [Online] Oxford University Press; 2017;65: S200–S219.
483 Available from: doi:10.1093/cid/cix664
- 484 42. UNICEF. *Adolescent health - UNICEF DATA*. [Online] Available from:
485 <https://data.unicef.org/topic/maternal-health/adolescent-health/> [Accessed: 13th February
486 2019]
- 487 43. The Prevention of Early-onset Neonatal Group B Streptococcal Disease in UK Obstetric Units.
488 2007; Available from:
489 [https://www.rcog.org.uk/globalassets/documents/guidelines/research--](https://www.rcog.org.uk/globalassets/documents/guidelines/research--audit/neonatal_audit_full_250507.pdf)
490 [audit/neonatal_audit_full_250507.pdf](https://www.rcog.org.uk/globalassets/documents/guidelines/research--audit/neonatal_audit_full_250507.pdf) [Accessed: 8th May 2018]
- 491 44. Roca A, Oluwalana C, Bojang A, Camara B, Kampmann B, Bailey R, et al. Oral azithromycin
492 given during labour decreases bacterial carriage in the mothers and their offspring: a double-
493 blind randomized trial. *Clinical Microbiology and Infection*. [Online] Elsevier; 2016;22(6):
494 565.e1-565.e9. Available from: doi:10.1016/j.cmi.2016.03.005 [Accessed: 23rd May 2018]
- 495 45. Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, et al. Global, regional, and national causes of
496 under-5 mortality in 2000–15: an updated systematic analysis with implications for the
497 Sustainable Development Goals. *The Lancet*. [Online] 2016;388(10063): 3027–3035. Available
498 from: doi:10.1016/S0140-6736(16)31593-8 [Accessed: 19th December 2018]
- 499 46. World population review. *Life Expectancy by Country 2017 - World Population Review*.
500 [Online] Available from: [http://worldpopulationreview.com/countries/life-expectancy-by-](http://worldpopulationreview.com/countries/life-expectancy-by-country/)
501 [country/](http://worldpopulationreview.com/countries/life-expectancy-by-country/) [Accessed: 12th February 2019]
- 502 47. GBDx. *Global Burden of Disease Study 2010 (GBD 2010) Disability Weights | GHDx*. [Online]
503 Available from: [http://ghdx.healthdata.org/record/global-burden-disease-study-2010-gbd-](http://ghdx.healthdata.org/record/global-burden-disease-study-2010-gbd-2010-disability-weights)
504 [2010-disability-weights](http://ghdx.healthdata.org/record/global-burden-disease-study-2010-gbd-2010-disability-weights) [Accessed: 24th May 2018]

505 48. Kim S-Y, Lee G, Goldie SJ. Economic evaluation of pneumococcal conjugate vaccination in The
506 Gambia. *BMC Infectious Diseases*. [Online] BioMed Central; 2010;10(1): 260. Available from:
507 doi:10.1186/1471-2334-10-260 [Accessed: 24th April 2018]

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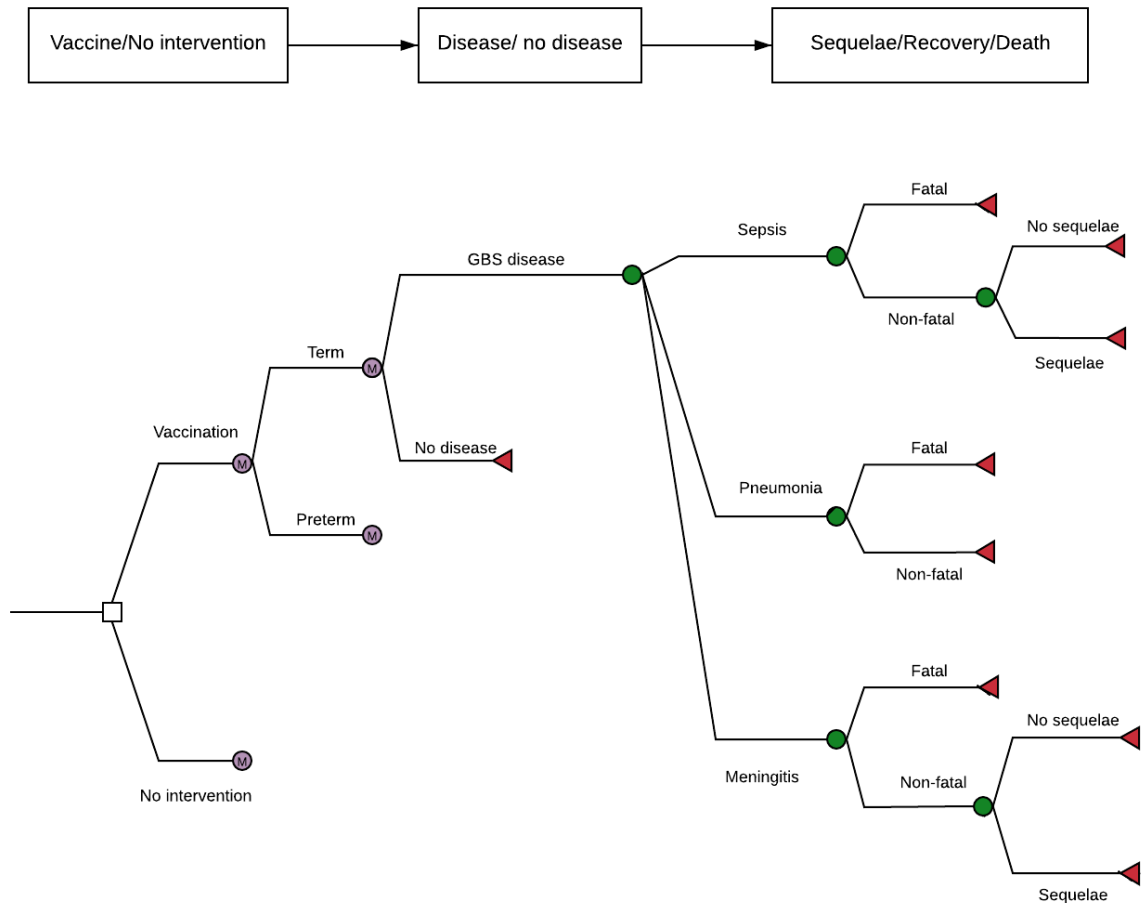
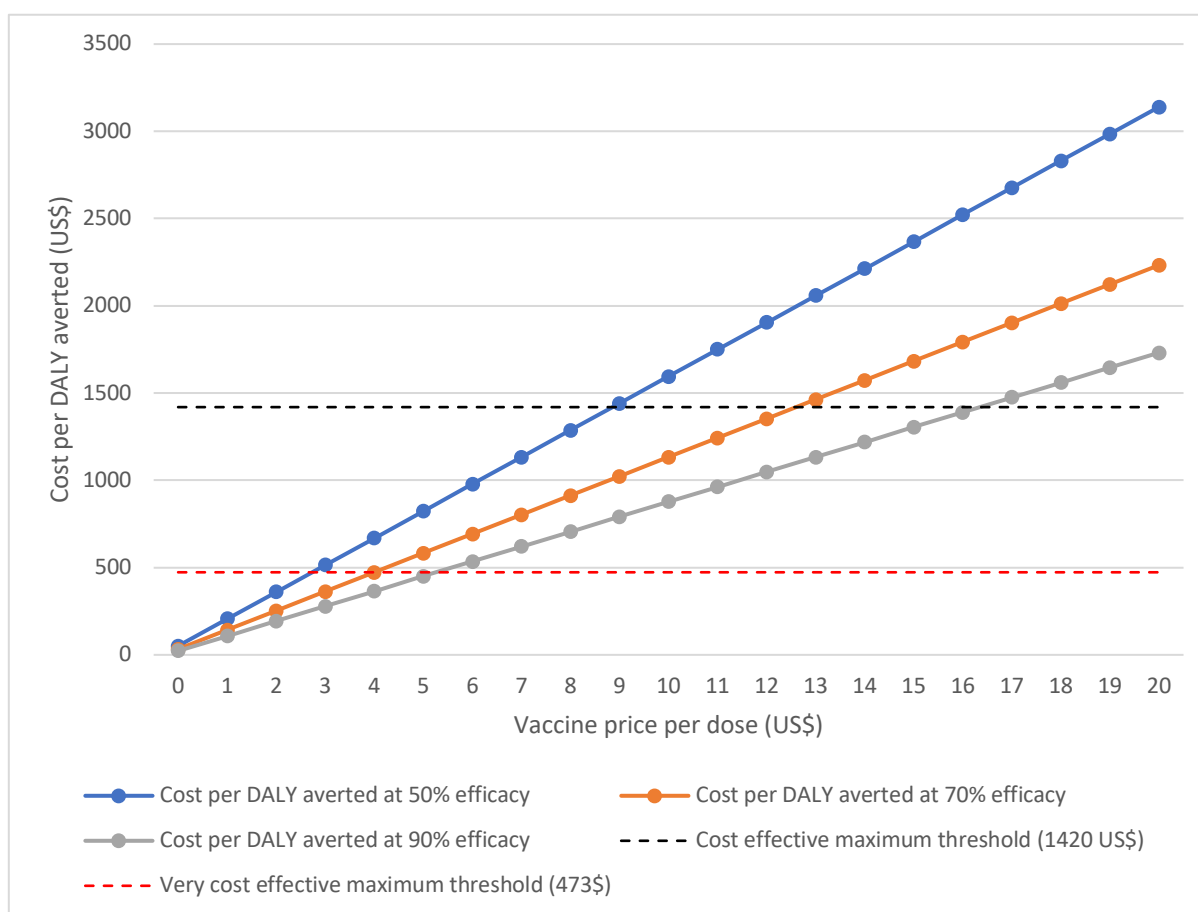


Figure 1: Decision tree for cost effectiveness analysis.

This diagram illustrates the two strategies in our model: the proposed Group B streptococcus (GBS) vaccination programme versus the current strategy of no intervention (no vaccination). Markov nodes denoted as M represent a continuation of the tree parallel to that of the other branch. For example, for both vaccination and no intervention, each livebirth can lead to GBS disease or no disease. GBS disease can present as sepsis, pneumonia or meningitis which can subsequently lead to death, disability or recovery.



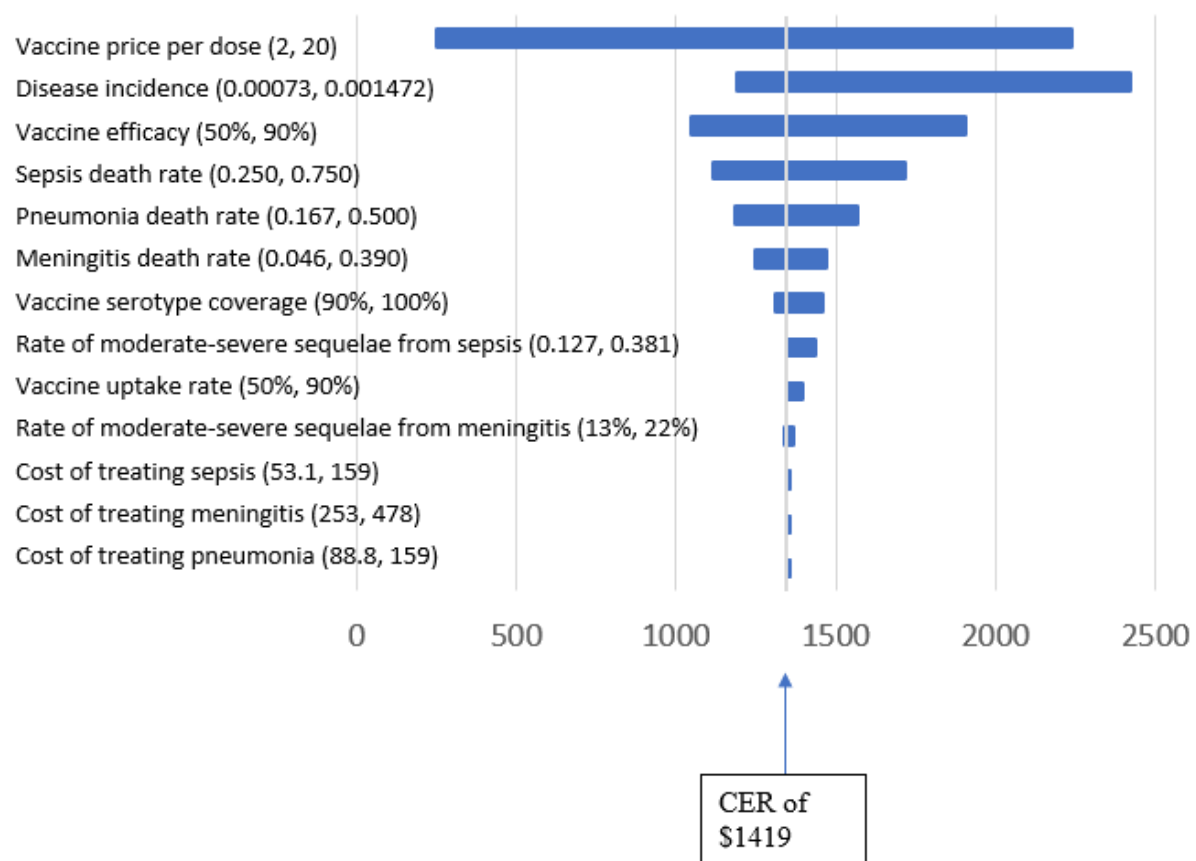
Figure

2: Incremental cost-effectiveness ratio of running models at vaccine efficacies 50%, 70% and 90%.

The maximum price per dose where the programme can be deemed cost effective (below the black hashed line) is \$8, \$12 and \$16 at vaccine efficacies 50%, 70% and 90% respectively. The programme is deemed very cost-effective (below the red hashed line) at a maximum vaccine price per dose of \$2, \$4 and \$5 at vaccine efficacies of 50, 70 and 90% respectively. DALY – disability adjusted life year; US\$ - American dollars.

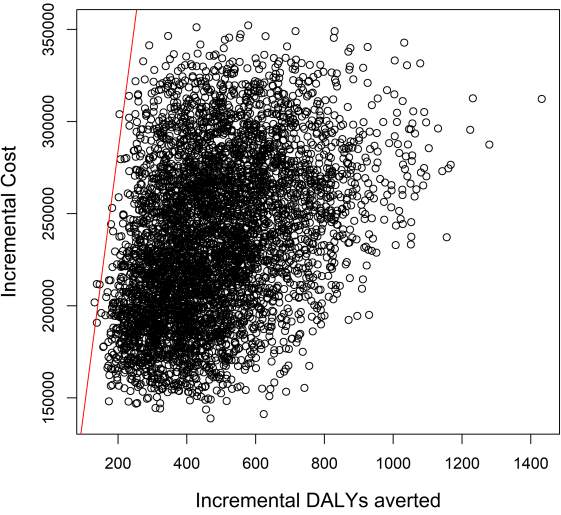
Figure 3: A tornado diagram illustrating the uncertainty associated with key parameters in the model.

Vaccine price per dose has the largest effect on the cost-effectiveness of the vaccination programme whereas out-of-pocket costs have the least effect. CER – cost-effectiveness ratio.



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Cost-effectiveness



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Figure 4a

Cost-effectiveness

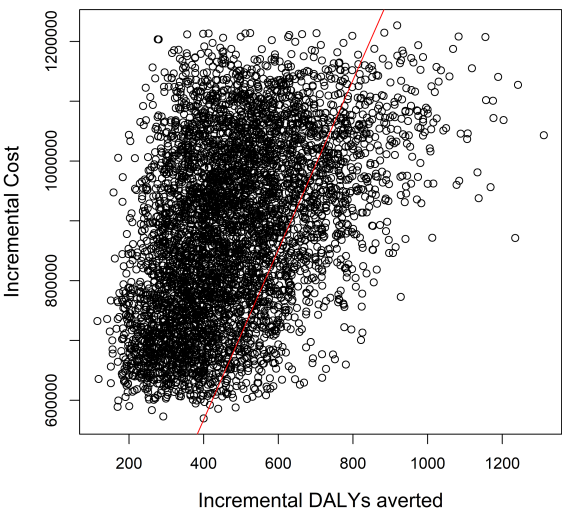
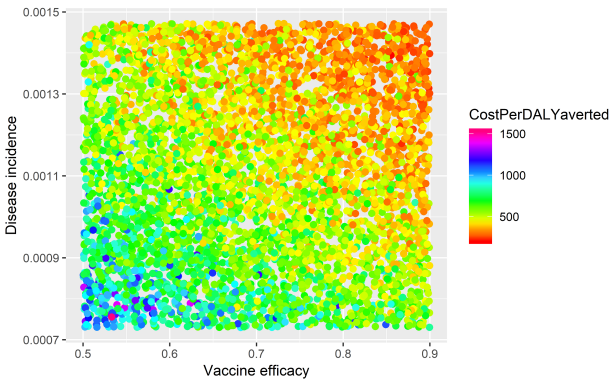


Figure 4b

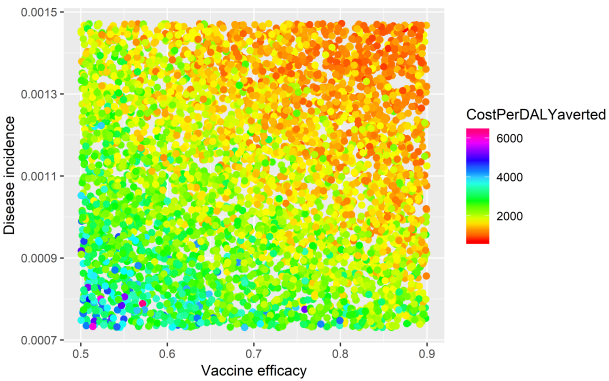
Figure 4: Monte Carlo probabilistic sensitivity analysis

Monte Carlo probabilistic sensitivity analysis of 23 parameters, 5000 iterations for base case scenario, for vaccine prices at \$3/dose (figure 5a) and \$12/dose (figure 5b). The incremental cost of the proposed immunisation strategy is plotted against the y axis with the x axis displaying the incremental DALYs averted. Of the 5000 iterations, 99.92% fall below the cost effectiveness threshold of \$1419.6 (red line) for the \$3/dose case, while 18.12% fall below this threshold when the price is \$12/dose. DALY – disability adjusted life year

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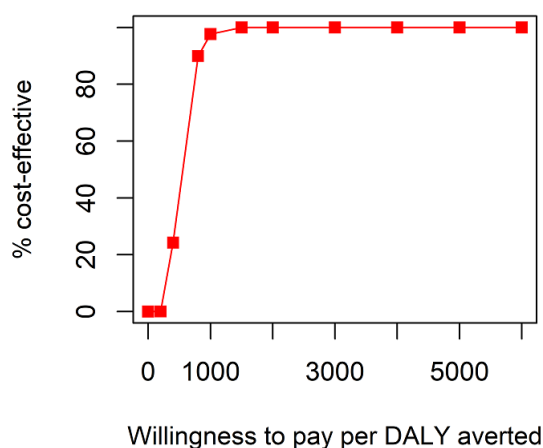
Figure 5a

Figure 5b

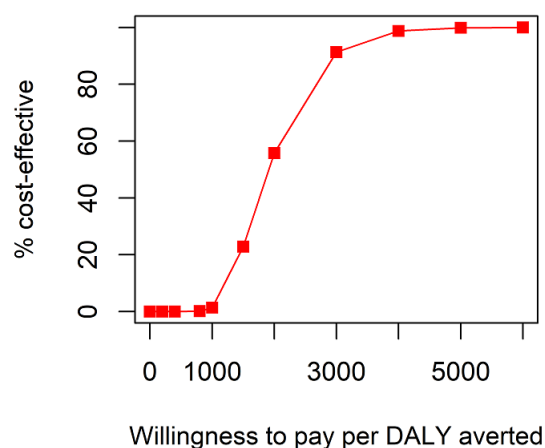
Figure 5: Comparison of disease incidence and vaccine efficacy as drivers of vaccine cost-effectiveness in terms of Cost per DALY averted.

The chart represents Monte Carlo probabilistic sensitivity analysis of 5000 iterations, where other parameter values remain as in base case scenario. Vaccine price per dose for the base case scenario is \$3 and \$12 respectively (top to bottom). The incremental cost (£) per DALY averted of the maternal immunisation strategy compared to no preventative strategy is represented by nodes of varying colour depending on value (colour guides on figure's right side). DALY: Disability-adjusted life year. DALY – disability adjusted life years.

Cost-effectiveness acceptability curve



Cost-effectiveness acceptability curve



556

Figure 6a

Figure 6b

Cost-effectiveness acceptability curve of the base case scenario (future costs and discount rate = 3%).

The graph displays the percentage of Monte Carlo iterations (total of 5000) for which the immunisation strategy is cost-effective, depending on the willingness of the healthcare system to pay

562 *(in \$) for each DALY averted. Vaccine price per dose in the base case scenario is \$3/dose (figure 6a)*
563 *and \$12/dose (figure 6b).*
564

565 **Table 1: demographic data, rates of each disease outcome and their associated disability weights,**
566 **vaccine parameters and costs associated with treatment and vaccination.**
567 *Their ranges are included as a reference for the sensitivity analysis. Each source is included with*
568 *relevant appendices, which include calculations of some parameters. ‘Local data’ refers to data from*
569 *the Gambian cohort of mother-infant pairs studied. GBS – Group B Streptococcus*
570

Parameter	Base-case value	Range	Distribution	Source
Birth in the Gambia (annual)				
Number of pregnancies	94,482	--	--	(12,32)
Number of livebirths	89,363	--	--	(32)
Number of stillbirths	4866	--	--	(12,45)
Number of preterm live births	9./ 804	--	--	(12,45)
Number of term livebirths	69196	--	--	(12,45)
Life expectancy	61	--	--	(46)
Reduced life expectancy of individuals with meningitis sequelae	30	--	Triangular (15,30,61)	(22)
Disease				
Neonatal GBS disease incidence per 1000 livebirths	1.3	0.73-1.472	Uniform	(12,17)
Rate of meningitis due to GBS	0.216	0.092-0.673	Uniform	(12,17)
Rate of sepsis due to GBS	0.431	0.216-0.647	Uniform	(12)
Rate of pneumonia due to GBS	0.353	0.177- 0.530	Uniform	(12)
Rate of sequelae from meningitis	0.18	0.13-0.22	Uniform	(19)
Rate of sequelae from sepsis survivors	0.369	0.127-0.381	Uniform	(17)
Death rate due to meningitis	0.213	0.046-0.390	Uniform	(18)
Death rate due to sepsis	0.500	0.250-0.750	Uniform	(16)
Death rate due to pneumonia	0.333	0.167-0.500	Uniform	(12)
Serotype coverage (%)	97	0.873, 0.97, 1	Triangular((12,30)
Vaccine				
Vaccine efficacy in term babies (%)	70	50-90	Uniform	(10,17)
Vaccine efficacy, preterm babies	83.1% of term (0.582)	0.416-0.748	--	(10,17) Appendix 3
Vaccine uptake rate	84.3%	0.5-0.9	Uniform	(12) Local data
In patient, provider treatment costs per case				
Meningitis	309	253-478	Gamma	(15) and (appendix)
Sepsis	106	53.1-159	Gamma	(15) and appendix
Pneumonia	111	88.8-155	Gamma	(15) and appendix
Family out of pocket costs				

Meningitis	56.2		-	(15) Appendix 4
Sepsis	45.3		-	(15) Appendix 4
Pneumonia	38.5		-	(15) Appendix 4
Meningitis sequelae	9.66	0-41.8	Uniform	(15) Appendix 4
Disability weights				
Meningitis sequelae ^c	0.260	0.153 - 0.364	Uniform	(21)
Sepsis sequelae ^d	0.221	0.141- 0.314	Uniform	(16,47)
Vaccine costs				
Vaccination programme administration costs per vaccinated woman (\$)	0.456	0- 0.912	Gamma	(48)
Vaccine wastage rate (%)	10	5-20	Uniform	(48)

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572

573 **Table 2: Health outcomes and costs before vaccine introduction and after introduction of a**
574 **vaccination programme at vaccine efficacies 50%, 70 and 90%.**

575 *The numbers of cases are categorised into those attributable to sepsis meningitis and pneumonia.*

576 *DALYs – Disability Adjusted Life Year; GBS – Group B Streptococcus; US\$ - American dollars.*

	No vaccine	Vaccine efficacy (%)		
		50	70	90
DALYs	1384	837	616	395
Number of disease cases	116	70	52	33
Cases averted, (% averted)		45.8	64.2 (55.5%)	82.7 (71.5%)
Meningitis cases	25	15	11	7
Sepsis cases	45	30	22	14
Pneumonia cases	41	25	18	12
Number of GBS deaths	44	27	20	13
Number of deaths averted, (% averted)		14 (32%)	24 (54.5%)	31 (70.5%)
Meningitis deaths	5	3	2	2
Sepsis deaths	25	15	11	7
Pneumonia deaths	14	8	6	4
Number of babies with sequelae	13	8	6	4
Number of sequelae averted, %		5 (40%)	7 (50%)	9 (71.5%)
Meningitis sequelae cases	4	2	2	1
Sepsis sequelae cases	9	6	4	3

Provider treatment costs (US\$)	17,542	10,604	7804	4837
Out-of-pocket costs for treatment (US\$)	5270	3186	2345	1453
Total treatment costs (US\$)	22,812	13,790	10,149	6290